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10/728,033	12/04/2003	Stephen F. Badylak	3220-73985	8358
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BARNES & THORNBURG LLP 11 SOUTH MERIDIAN INDIANAPOLIS, IN 46204				SCHUBERG, LAURA J
ART UNIT		PAPER NUMBER		
1657				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

indocket@btlaw.com

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/728,033	BADYLAK, STEPHEN F.	
	<b>Examiner</b>	<b>Art Unit</b>	
	LAURA SCHUBERG	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 16 March 2010.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-16 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-16 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ .	5) <input type="checkbox"/> Notice of Informal Patent Application
	6) <input type="checkbox"/> Other: _____ .

## DETAILED ACTION

This action is responsive to papers filed 03/16/2010. Claim 1 was amended. No claims were newly added or newly canceled.

Claims 1-16 are currently pending.

### ***Previous Rejections***

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**Claims 1-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Badylak (WO 98/25637) in view of Patel et al (US 5,955,110), Butler (WO 03/084410) and Oliver et al (US 4,399,123).**

Amended claim 1 is drawn to a method for inducing the repair of damaged or diseased body wall tissues comprising the steps of preparing a graft composition consisting essentially of basement membrane of a warm-blooded vertebrate by removing endogenous cells, DNA and endotoxins from the graft; wherein the graft is administered to a patient in an amount effective to induce repair, wherein the body wall tissue comprises a multilaminate, stratified structure comprising different tissue types including connective tissue, skeletal muscle, adipose tissue, epidermal tissue and the serous lining of the body wall cavity, and wherein the graft composition comprises a glycoprotein.

Dependent claims include the site of repair, wherein the graft is multi-layered, thickness of the layers, format of the layers, administration type and form, sterilization of the graft, addition of growth factors, and seeding with exogenous cells.

The transitional phrase “consisting essentially of” limits the scope of a claim to the specified materials or steps “and those that do not materially affect the basic and novel characteristic(s)” of the claimed invention. For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the

specification or claims of what the basic and novel characteristics actually are, “consisting essentially of” will be construed as equivalent to “comprising.” Although ‘consisting essentially of’ is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant’s burden to establish that a step practiced in a prior art method is excluded from his claims by consisting essentially of language. (see MPEP 2105).

Badylak ('637) teaches the use of tissue graft composition comprising liver basement membranes of a warm-blooded vertebrate for the repair of damaged or diseased tissues (page 2 lines 1-6). The preparation involves the removal of cells and cellular components from the liver tissue (page 3 lines 3-32) and since this includes the same method steps as taught in the instant application for the removal of DNA and endotoxins (page 4 of the specification) this reference process will also remove DNA and endotoxins as well (page 3 lines 3-32). The graft composition can be implanted or fluidized and injected into a host to contact damaged or defective tissues and induce repair or replacement of the tissues (page 2 lines 6-8). Wherein the composition is in the form of a powder (page 4 line 22), sheet (patch) or gel (page 10 lines 20-21) is taught as well as wherein the composition is in a multilayered configuration (page 6 line

31) with sheets or strips having a thickness of up to about 500  $\mu$  (page 17 line 14). Sterilization of the composition by peracetic acid is taught as most preferred (page 5 lines 20-28). The composition has a honeycomb-like structure (page 10 lines 24-25) and this is interpreted as perforated. The reference includes wherein growth factors and glycoproteins that facilitate cellular proliferation are added to the composition (page 11 lines 16-20) as well as the seeding with various exogenous cell types (page 12 lines 20-28) for the same reasons as described by Applicant's specification (page 13).

In addition, Badylak ('637) teaches that basement membrane prepared from liver tissue of warm-blooded vertebrates exhibit certain mechanical and biotropic properties similar to that which had been reported for intestinal submucosal tissue. The reference also states that liver basement membrane can be substituted in most, if not all, of the applications previously reported for intestinal submucosa, including enhancing wound healing, promoting endogenous tissue growth, stimulating cell proliferation and inducing cell differentiation (page 1 lines 16-24). These applications would all be required for the repair of the body wall. Wherein the construct is taught to have multiple layers at the opposite ends (thus forming a heterolaminate construct) to provide reinforcement for attachment to physiological structures such as bone, tendon, ligament, cartilage and muscle (page 6 line 32- page 7 line 4) is also taught to be an optional embodiment since the liver basement graft composition can be formed in a variety of shapes and configurations (page 6 line 28).

Badylak ('637) does not specifically teach wherein the body wall tissue to be repaired comprises the abdominal wall or wherein the graft composition is formed as a multilayered homolaminate construct.

Oliver et al teach a method wherein basement membrane is used various branches of surgery for the treatment of hernias (column 1 lines 55-66 and column 5 lines 60-62).

Butler teaches that basement membrane is a suitable material for repair of body wall tissues such as hernias (paragraphs 16, 21, 76-84, on pages 8, 10, 30-33).

Patel teaches a multilayered submucosal graft construct for use in hernia repair, gastroschisis repair (congenital stomach defects) and other types of body wall repairs that require larger sheets of graft material (column 1 lines 60-65). Small intestinal tissue is taught as the source of the submucosal tissue (column 3 lines 26-27). Patel also teaches that advantageously, both the heterolaminar and homolaminar large area sheets of submucosal tissue have enhanced mechanical strength and have a greater surface area than any one of the individual strips used to form the submucosal sheets (column 5 lines 18-23).

Therefore, one of ordinary skill in the art would have been motivated to use the invention of Badylak ('637) for the repair of the abdominal wall because Patel teaches that a multilayered submucosal graft can be used in hernia repair and other applications that would include the abdominal wall and because Badylak ('637) also teaches that liver basement membrane can be used in most, if not all, of the applications previously reported for intestinal submucosa, including enhancing wound healing, promoting

endogenous tissue growth, stimulating cell proliferation and inducing cell differentiation (page 1 lines 16-24). One of ordinary skill in the art would have had a reasonable expectation of success because Oliver et al and Butler teach the use of basement membrane in hernia repair (column 5 lines 60-65).

In addition, one of ordinary skill in the art would have been motivated to use the multilayered homolaminate construct because Patel teaches that both the heterolaminar and homolaminar large area sheets of submucosal tissue have enhanced mechanical strength and have a greater surface area than any one of the individual strips used to form the submucosal sheets (column 5 lines 18-23) and Badylak ('637) teaches that heterolaminar constructs (those with extra layers at the ends) are preferable for reinforcement for attachment to bone and other structures (page 7 line 2) and thus would not be required when used for abdominal wall repair. A homolaminate construct would be an obvious choice for repair of the abdominal wall repair since attachment to bones, tendons, ligaments, cartilage and muscle would not be required (only attachment to the body wall) and a step would be saved by not having to form the additional layers on the ends as required by the heterolaminar construct. One of ordinary skill in the art would have had a reasonable expectation of success because Badylak ('637) teaches that the liver basement graft composition can be formed in a variety of shapes and configurations (page 6 line 28).

Therefore, the combined teachings of Badylak, Patel, Butler and Oliver et al render obvious Applicant's invention as claimed.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 1-16 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11 of U.S. Patent No. 7,482,025 in view of Patel et al (US 5,955,110), Badylak (WO 98/25637), Butler (WO 03/084410) and Oliver et al (US 4,399,123).**

Although the conflicting claims are not identical, they are not patentable distinct from each other because the patented claim is drawn to a method for inducing the formation of endogenous tissue at a site in need in a warm-blooded vertebrate comprising implanting a graft composition comprising gelled liver basement membrane

tissue of a warm-blooded vertebrate at the site in need in an amount effective and further comprises a glycoprotein.

The '025 Patent does not include wherein the body wall or abdominal wall is the site of repair or wherein the construct is multilayered, the thickness of the layers or wherein the construct is formed as a homolaminate. Wherein the construct is in a sheet form and surgically implanted or in powder form is also not included.

Patel teaches a multilayered submucosal graft construct for use in hernia repair, gastroschisis repair (congenital stomach defects) and other types of body wall repairs that require larger sheets of graft material (column 1 lines 60-65). Small intestinal tissue is taught as the source of the submucosal tissue (column 3 lines 26-27). Patel also teaches that advantageously, both the heterolaminar and homolaminar large area sheets of submucosal tissue have enhanced mechanical strength and have a greater surface area than any one of the individual strips used to form the submucosal sheets (column 5 lines 18-23).

Badylak ('637) teaches the use of tissue graft composition comprising liver basement membranes of a warm-blooded vertebrate for the repair of damaged or diseased tissues (page 2 lines 1-6). The graft composition can be implanted or fluidized and injected into a host to contact damaged or defective tissues and induce repair or replacement of the tissues (page 2 lines 6-8). Wherein the composition is in the form of a powder (page 4 line 22), sheet or gel (page 10 lines 20-21) is taught as well as wherein the composition is in a multilayered configuration (page 6 line 31) with sheets or strips having a thickness of up to about 500  $\mu$  (page 17 line 14). Badylak ('637) also

teaches that basement membrane prepared from liver tissue of warm-blooded vertebrates exhibit certain mechanical and biotropic properties similar to that which had been reported for intestinal submucosal tissue. The reference also states that liver basement membrane can be substituted in most, if not all, of the applications previously reported for intestinal submucosa, including enhancing wound healing, promoting endogenous tissue growth, stimulating cell proliferation and inducing cell differentiation (page 1 lines 16-24). These applications would all be required for the repair of the body wall. Wherein the construct is taught to have multiple layers at the opposite ends (thus forming a heterolaminate construct) to provide reinforcement for attachment to physiological structures such as bone, tendon, ligament, cartilage and muscle (page 6 line 32- page 7 line 4) is also taught to be an optional embodiment since the liver basement graft composition can be formed in a variety of shapes and configurations (page 6 line 28). The reference includes wherein growth factors and glycoproteins that facilitate cellular proliferation are added to the composition (page 11 lines 16-20).

Oliver et al teach a method wherein basement membrane is used various branches of surgery for the treatment of hernias (column 1 lines 55-66 and column 5 lines 60-62).

Butler teaches that basement membrane is a suitable material for repair of body wall tissues such as hernias (paragraphs 16, 21, 76-84, on pages 8, 10, 30-33).

Therefore, one of ordinary skill in the art would have been motivated to use the method of the copending application for the repair of the abdominal wall because Patel teaches that a multilayered submucosal graft can be used in hernia repair and other

applications that would include the abdominal wall and because Badylak ('637) also teaches that liver basement membrane can be used in most, if not all, of the applications previously reported for intestinal submucosa, including enhancing wound healing, promoting endogenous tissue growth, stimulating cell proliferation and inducing cell differentiation (page 1 lines 16-24). One of ordinary skill in the art would have had a reasonable expectation of success because Badylak ('637) reports that basement membranes prepared from liver tissue of warm-blooded vertebrates exhibit certain mechanical and biotropic properties similar to that which had been reported for intestinal submucosal tissue (page 1 lines 15-20) and Butler teaches that basement membrane is a suitable material for the repair of the body wall.

In addition, one of ordinary skill in the art would have been motivated to use the multilayered homolaminate construct because Patel teaches that both the heterolaminar and homolaminar large area sheets of submucosal tissue have enhanced mechanical strength and have a greater surface area than any one of the individual strips used to form the submucosal sheets (column 5 lines 18-23) and Badylak ('637) teaches that heterolaminar constructs (those with extra layers at the ends) are preferable for reinforcement for attachment to bone and other structures (page 7 line 2) and thus would not be required when used for abdominal wall repair. A homolaminate construct would be an obvious choice for repair of the abdominal wall repair since attachment to bones, tendons, ligaments, cartilage and muscle would not be required (only attachment to the body wall) and a step would be saved by not having to form the additional layers on the ends as required by the heterolaminar construct. The use of different forms such

as multilayered, powder and sheet would have been obvious to include in the copending application because Badylak and Patel teach that these are suitable forms for the construct. The thickness of the layers of the construct would have been a matter of routine optimization depending on the thickness of the body wall in need of repair. One of ordinary skill in the art would have had a reasonable expectation of success because Badylak ('637) teaches that the liver basement graft composition can be formed in a variety of shapes and configurations (page 6 line 28).

Therefore, the combined teachings of the patented claims and Badylak, Patel, Butler and Oliver et al render obvious Applicant's invention as claimed.

**Claims 1-16 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 9 of U.S. Patent No. 6,793,939 in view of Patel et al (US 5,955,110), Badylak (WO 98/25637), Butler (WO 03/084410) and Oliver et al (US 4,399,123).**

Although the conflicting claims are not identical, they are not patentable distinct from each other because the patent is drawn to a method for inducing the formation of endogenous tissue at a site in need in a warm-blooded vertebrate comprising implanting a graft composition comprising an extracellular matrix consisting essentially of basement membrane of liver tissue of a warm blooded vertebrate in an amount effective to induce endogenous tissue growth at the site of administration. Wherein the basement membrane is fluidized and administered by injection and administered by surgically

implanting and wherein the liver tissue is in sheets having a thickness of up to about 500  $\mu$  are also included.

The claims of the patent do not include wherein the body wall or abdominal wall is the site of repair or wherein the construct is multilayered, or wherein the construct is formed as a homolaminate. Wherein the construct is in a sheet form and surgically implanted or in powder form is also not included.

Patel teaches a multilayered submucosal graft construct for use in hernia repair, gastroschisis repair (congenital stomach defects) and other types of body wall repairs that require larger sheets of graft material (column 1 lines 60-65). Small intestinal tissue is taught as the source of the submucosal tissue (column 3 lines 26-27). Patel also teaches that advantageously, both the heterolaminar and homolaminar large area sheets of submucosal tissue have enhanced mechanical strength and have a greater surface area than any one of the individual strips used to form the submucosal sheets (column 5 lines 18-23).

Badylak ('637) teaches the use of tissue graft composition comprising liver basement membranes of a warm-blooded vertebrate for the repair of damaged or diseased tissues (page 2 lines 1-6). The graft composition can be implanted or fluidized and injected into a host to contact damaged or defective tissues and induce repair or replacement of the tissues (page 2 lines 6-8). Wherein the composition is in the form of a powder (page 4 line 22), sheet or gel (page 10 lines 20-21) is taught as well as wherein the composition is in a multilayered configuration (page 6 line 31) with sheets or strips having a thickness of up to about 500  $\mu$  (page 17 line 14). Badylak ('637) also

teaches that basement membrane prepared from liver tissue of warm-blooded vertebrates exhibit certain mechanical and biotropic properties similar to that which had been reported for intestinal submucosal tissue. The reference also states that liver basement membrane can be substituted in most, if not all, of the applications previously reported for intestinal submucosa, including enhancing wound healing, promoting endogenous tissue growth, stimulating cell proliferation and inducing cell differentiation (page 1 lines 16-24). These applications would all be required for the repair of the body wall. Wherein the construct is taught to have multiple layers at the opposite ends (thus forming a heterolaminate construct) to provide reinforcement for attachment to physiological structures such as bone, tendon, ligament, cartilage and muscle (page 6 line 32- page 7 line 4) is also taught to be an optional embodiment since the liver basement graft composition can be formed in a variety of shapes and configurations (page 6 line 28). The reference includes wherein growth factors and glycoproteins that facilitate cellular proliferation are added to the composition (page 11 lines 16-20).

Oliver et al teach a method wherein basement membrane is used various branches of surgery for the treatment of hernias (column 1 lines 55-66 and column 5 lines 60-62).

Butler teaches that basement membrane is a suitable material for repair of body wall tissues such as hernias (paragraphs 16, 21, 76-84, on pages 8, 10, 30-33).

Therefore, one of ordinary skill in the art would have been motivated to use the method of the patent for the repair of the abdominal wall because Patel teaches that a multilayered submucosal graft can be used in hernia repair and other applications that

would include the abdominal wall and because Badylak ('637) also teaches that liver basement membrane can be used in most, if not all, of the applications previously reported for intestinal submucosa, including enhancing wound healing, promoting endogenous tissue growth, stimulating cell proliferation and inducing cell differentiation (page 1 lines 16-24). One of ordinary skill in the art would have had a reasonable expectation of success because Badylak ('637) reports that basement membranes prepared from liver tissue of warm-blooded vertebrates exhibit certain mechanical and biotropic properties similar to that which had been reported for intestinal submucosal tissue (page 1 lines 15-20) and Butler teaches that basement membrane is suitable for repair of the body wall as well.

In addition, one of ordinary skill in the art would have been motivated to use the multilayered homolaminate construct because Patel teaches that both the heterolaminar and homolaminar large area sheets of submucosal tissue have enhanced mechanical strength and have a greater surface area than any one of the individual strips used to form the submucosal sheets (column 5 lines 18-23) and Badylak ('637) teaches that heterolaminar constructs (those with extra layers at the ends) are preferable for reinforcement for attachment to bone and other structures (page 7 line 2) and thus would not be required when used for abdominal wall repair. A homolaminate construct would be an obvious choice for repair of the abdominal wall repair since attachment to bones, tendons, ligaments, cartilage and muscle would not be required (only attachment to the body wall) and a step would be saved by not having to form the additional layers on the ends as required by the heterolaminar construct. The use of different forms such

as multilayered, powder and sheet would have been obvious to include in the copending application because Badylak and Patel teach that these are suitable forms for the construct. One of ordinary skill in the art would have had a reasonable expectation of success because Badylak ('637) teaches that the liver basement graft composition can be formed in a variety of shapes and configurations (page 6 line 28).

One of ordinary skill in the art would have been motivated with a reasonable expectation of success in adding glycoproteins to the basement membrane composition as Badylak ('637) suggest that these facilitate cellular proliferation (page 11).

Therefore, the combined teachings of the patent claims and Badylak, Patel, Butler and Oliver et al render obvious Applicant's invention as claimed.

### ***Response to Arguments***

Applicant's arguments filed 03/16/2010 have been fully considered but they are not persuasive.

Applicant argues that the '123 patent can not be properly combined with the WO 98/25637 document because the '123 patent teaches the removal of the glycoproteins and thus teaches away from the WO 98/25637 and the current claimed invention which require glycoproteins. Applicant argues that the '123 patent states that glycoproteins are antigenic and their removal is required to create a fibrous tissue composition that is suitable for implantation.

This is not found persuasive because the WO 98/25637 teaches enzymatic cell removal steps (page 4) and extraction steps (page 5) that also removes glycoproteins, but also states that proteins, including glycoproteins, that facilitate cellular proliferation can be added back into the basement composition (page 11 lines 16-20). The '123 patent only suggests the removal of those glycoproteins that would cause an antigenic response, not that glycoproteins could not be added back in to the composition as suggested by WO 98/25637. Clearly this demonstrates that many antigenic components (cells, glycoproteins, growth factors) are removed during the preparation of the basement membrane and then new components added back in a form more suitable for the intended method of repair. Therefore the reference teachings are compatible for combination as the '123 patent does not require that glycoproteins that do not elicit an immune response (such as those added back into the composition as taught by WO 98/25637) be absent from the final composition. The sole purpose in removing these proteins is to avoid an antigenic response in the recipient. Clearly the use of glycoproteins that are either native to the recipient or are of recombinant origin would satisfy the requirements of both reference methods. In addition the teaching of Butler further demonstrates that basement membrane was known in the prior art to be a suitable material for the repair of the body wall (hernia repair) as well.

Applicant argues that in column 3 lines 8-18, the '123 patent states that, even for transplants between individuals within a species, "such carbohydrate material may not be significantly antigenic, nevertheless it does not contribute to the strength of the tissue and may severely obstruct the subsequent recolonization of the graft by host cells, such

as fibroblasts, and interfere with the formation of new capillaries within the graft".

Applicant asserts that this is evidence that the '123 patent teaches away from a graft composition comprising glycoproteins.

This is not found persuasive because the passage that Applicant has cited refers to the inclusion of mucopolysaccharides such as hyaluronic acid and also polysaccharides (column 3 lines 8-12). Glycoproteins that facilitate cellular proliferation, such as those suggested by WO 98/25637 (page 11 lines 16-19), are not referred to in this passage.

Applicant argues that the Butler reference (WO 03/084410) teaches away from the present invention because the current claims require a graft composition that consists essentially of basement membrane for the repair of body wall tissue and the reference method includes additional materials to produce their graft.

This is not found persuasive for two reasons. First, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). It is clear from these references that the basement membrane graft material of WO 98/25637 is a suitable choice for the repair of body wall tissue. Second, as stated above the transitional phrase "consisting essentially of" is interpreted as comprising for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103.

Applicant argues that in the Butler reference even though a barrier material (e.g. basement membrane) can function as a support material that two or more different biodegradable barrier materials are required. Applicant asserts that this is evidence that the Butler reference teaches away from Applicant's claimed invention which consists essentially of basement membrane for the repair of body wall tissue.

This is not found persuasive because the Butler reference states that a barrier material can be used alone or in combination with any other suitable barrier materials as will be recognized by one of skill in the art (page 17, paragraph 41). More than one layer of barrier material can be used to make up the composite and the layers can be made from the **same material** or combination of materials, or the layers can be made from different suitable materials (pages 19-20, paragraph 48). Therefore an embodiment wherein the support material and the barrier material are both basement membrane is supported by the Butler reference as well as two or more different barrier materials are clearly not required.

Applicant argues that the references do not suggest the specific element of removing endotoxins from the graft compositions and thus do not render obvious the claimed invention.

This is not found persuasive because the WO 98/25637 document specifically states that the process of removing the cellular elements from the tissue allows the preparation of a graft composition that is non-immunogenic, and thus does not induce a host immune response when implanted into a host (page 3 lines 3-10). Clearly this process would also remove any endotoxins as well as they would also elicit an immune

response if left with the tissue. Applicant's disclosure also suggests that the process of removing the cellular components also removes the endotoxins as well (page 4 lines 18-25 of the as filed specification). The reference process involves the removal of cells and cellular components from the liver tissue (page 3 lines 3-32) and since this includes the same method steps as taught in the instant application for the removal of DNA and endotoxins (page 4 of the specification) this reference process will also remove DNA and endotoxins as well (page 3 lines 3-32).

Applicant's arguments with regard to the double patenting rejections are identical to those presented above and are therefore also not found persuasive as well.

Therefore the claims remain rejected as obvious over the prior art.

### ***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/  
Primary Examiner, Art Unit 1651

Laura Schuberg